Does higher body mass index worsen efavirenz-based antiretroviral therapy's negative impact on the contraceptive implant's effectiveness among HIV-positive women?

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Background

- Preventing unintended pregnancies is critical among all women, including HIV-positive women
  - Subdermal implants are the most effective form of contraception, with pregnancy rates <1%[1,2]
- Implant's effectiveness is reduced by concomitant efavirenz-based ART use
  - 3 times higher rates of pregnancies with implants and efavirenz- vs. nevirapine-based ART (though these rates are still lower than pregnancies with most other contraceptives)[3]
- Higher body mass index (BMI) may further reduce implant effectiveness when combined with efavirenz
  - Higher BMI is associated with lower plasma implant concentrations[4,5]
  - Higher BMI may reductive effectiveness of contraceptives[6]

Methods

- Cohort analysis of HIV-positive women in Western Kenya
  - Enrolled in care at FACES, a HIV treatment program supported by CDC/PEPFAR
  - Aged 15-45 years, followed from January 2011 to December 2013
  - 3,457 women using implants contributed 5,885 person-years and 84 incident pregnancies
- Primary outcome: incident pregnancy (diagnosed clinically)
- Primary exposures:
  - ART regimen (efavirenz-, nevirapine-based ART, and no ART)
  - BMI (underweight: BMI≤18.5, normal weight: BMI≥18.5 but <25, and overweight: BMI≥25 and <30)
- Used robust Poisson models to generate pregnancy rates and rate ratios
  - Adjusted for repeated measures and age

Results

Table 1. Incident pregnancy rates and rate ratios, by ART regimen and BMI categories

	Pregnancies/person-years	Unadjusted Pregnancy Rate, per 100 person-years (95% CI)	Unadjusted IRR (95% CI)*	Adjusted IRR (95% CI)**
Efavirenz-based ART				
Underweight	3/56.7	5.3 (1.7, 16.4)	0.97 (0.28, 3.32)	1.02 (0.29, 3.56)
Normal weight	15/270.2	5.6 (3.3, 9.2)	ref	ref
Overweight	5/69.0	4.3 (1.4, 13.5)	0.79 (0.17, 3.79)	0.88 (0.18, 4.22)
Nevirapine-based ART				
Underweight	2/201.8	1.0 (0.2, 4.0)	0.45 (0.11, 1.86)	0.42 (0.10, 1.74)
Normal weight	28/1259.3	2.2 (1.5, 3.2)	ref	ref
Overweight	4/282.4	1.4 (0.5, 3.8)	0.64 (0.22, 1.82)	0.64 (0.22, 1.82)
No ART				
Underweight	2/84.1	2.4 (0.6, 9.5)	0.65 (0.16, 2.71)	0.63 (0.15, 2.63)
Normal weight	25/679.6	3.7 (2.5, 5.4)	ref	ref
Overweight	2/175.1	1.1 (0.3, 4.6)	0.30 (0.07, 1.29)	0.33 (0.08, 1.37)

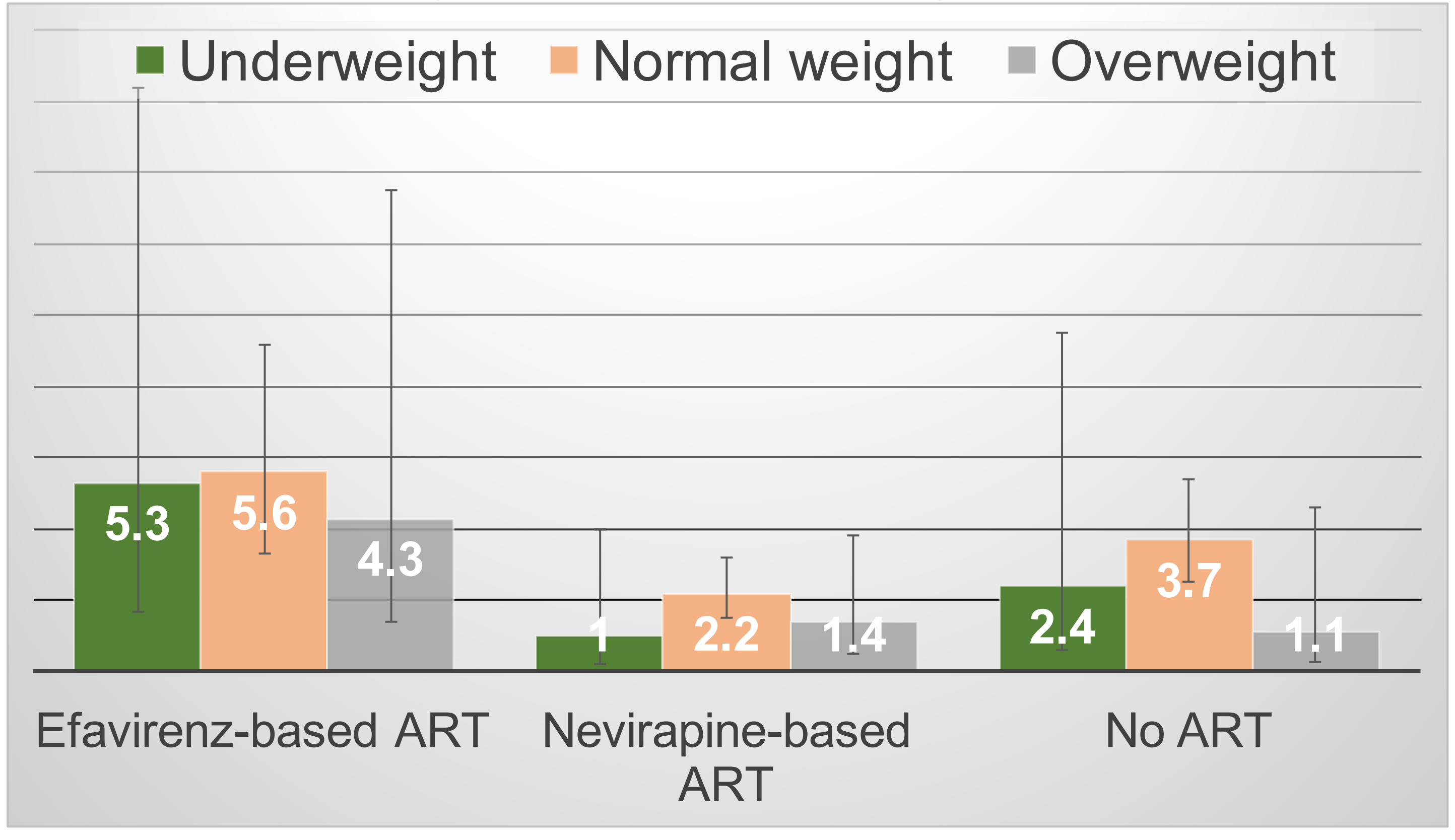
* Wald test for the BMI x ART interaction p>0.05. ** Wald test for the BMI x ART interaction p>0.05. Adjusted for age.

Table 2. Incident pregnancy rates and rate ratios, by ART regimen and weight categories

	Pregnancies/person-years	Unadjusted Pregnancy Rate, per 100 person-years (95% CI)	Unadjusted IRR (95% CI)*	Adjusted IRR (95% CI)**
Efavirenz-based ART				
<70kg	20/362.7	5.5 (3.6, 8.5)	ref	ref
≥70kg	1/41.8	2.4 (0.3, 17.0)	0.43 (0.06, 3.29)	0.55 (0.07, 4.14)
Nevirapine-based ART				
<70kg	31/1573.3	2.0 (1.4, 2.8)	ref	ref
≥70kg	3/228.0	1.3 (0.4, 4.1)	0.67 (0.20, 2.18)	0.73 (0.22, 2.39)
No ART				
<70kg	28/840.4	3.3 (2.3, 4.8)	ref	ref
≥70kg	1/139.2	0.7 (0.1, 5.1)	0.21 (0.03, 1.59)	0.25 (0.03, 1.85)

* Wald test for the BMI x ART interaction p>0.05. ** Wald test for the BMI x ART interaction p>0.05. Adjusted for age.

Figure 1. Incident pregnancy rate ratios, by ART regimen and BMI categories



Conclusions

- No association between higher BMI and worsening effect of efavirenz-based ART on pregnancy incidence among implant users
  - HIV-positive women should continue to be offered implants if on efavirenz-based ART, in accordance with current WHO guidelines[7]
- Greater follow-up, esp. of overweight and obese women, is needed to better evaluate BMI's affect

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